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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/098,642	03/15/2002	Tiecheng A. Qiao	84027WFN	7342

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/098,642	QIAO ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *03/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains, on page 8, an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification is further objected to because it contains two tables, each of which is labeled and identified in the text as "Table 1" (see pages 15 and 19).

The specification is also objected to because it contains nucleic acid sequences which are not identified by a "SEQ ID NO:" (see the table on page 19).

Appropriate correction is required.

Claim Objections

2. Claim 2 is objected to because the "sub-population" of line 2 and the "obtain" should be in plural form i.e. "sub-populations" and "obtains".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-20 are indefinite in Claim 1 because the claim is drawn to a method of identifying nucleic acid sample but the claim does not recite method steps of sample identification. Therefore the claims are indefinite, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: nucleic acid sample identification.

b. Claims 1-20 are indefinite in Claim 1, line 6, for the recitation "the gelatin coating" because "gelatin" and "gelatin coating" lack proper antecedent basis in the claim. It is suggested that Claim 1 be amended to provide proper antecedent basis.

c. Claims 1-20 are indefinite in Claim 1, lines 10 and 14, for the recitation "fluorescently/chemiluminescently labeled nucleic acid" because it is unclear whether the label comprises both or alternatively fluorescence and chemiluminescence. It is suggested that Claim 1 be amended to clarify.

d. Claims 1-20 are indefinite in Claim 1, line 12, for the recitation "the color barcode" because the recitation lacks proper antecedent basis in the "optical barcode" of line 8. It is suggested that Claim 1 be amended to provide proper antecedent basis.

e. Claims 5 and 6 are indefinite in Claim 5 for the recitation "the luminescent image" because the recitation lacks proper antecedent basis in the claim. It is suggested that Claim 5 be amended to provide proper antecedent basis.

f. Claim 20 is indefinite because it is unclear whether the recitation is intended as an additional method step for the method of Claim 1 or whether the recitation is intended to define a physical and/or structural property of the microsphere.

g. Claims 21-25 are indefinite in Claim 21, line 10, for the recitation "the color barcode" because the recitation lacks proper antecedent basis in the "optical bar" of line 5. It is suggested that Claim 21 be amended to provide proper antecedent basis.

h. Claims 21-25 are indefinite in Claim 21, lines 8 and 12, for the recitation "fluorescently/chemiluminescently labeled nucleic acid" because it is unclear whether the label comprises both or alternatively fluorescence and chemiluminescence. It is suggested that Claim 21 be amended to clarify.

i. Claims 21-25 are indefinite in Claim 21, step (a), for the recitation "the luminescent for fluorescent image" because the recitation lacks proper antecedent basis in the claim. It is suggested that Claim 21 be amended to provide proper antecedent basis.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Walt et al (WO 00/16101, published 23 March 2000).

Regarding Claim 21, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a

population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a fluorescently labeled target sequence (page 29, Table V) and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) wherein at least one subpopulation has a luminescent property (i.e. fluorescence) and wherein detecting includes whole frame imaging capture of a resulting luminescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 22, Walt et al disclose the method wherein said processing uses a pattern recognition algorithm to obtain the identification (page 32, line 5-page 35, line 12).

Regarding Claim 23, Walt et al disclose the method wherein each subpopulation has a unique optical signature (bar code) and a unique probe sequence (page 17, lines 15-19).

Regarding Claim 24, Walt et al disclose the method wherein the optical bar code is generated by two or more colorants i.e. each optical signature is comprises of a mixture of dyes (page 16, liens 25-28).

Regarding Claim 25, Walt et al disclose the method wherein the optical barcode is generated by a mixture of red, green and blue i.e. each optical signature is comprises of a

mixture of dyes including red, green and blue dyes e.g. rhodamine, Malacite green, and Cascade Blue™ (page 16, line 25-page 17, line 2).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in view of Seul et al (U.S. Patent Application Publication No. 2003/0138842 A1 having priority to 60/300,025 filed 21 June 2001) .

Regarding Claim 1, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array

with a fluorescently labeled target sequence (page 29, Table V) and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11). Walt et al further teach that their method requires permeability of the gelling agent (page 22, lines 20-22) which suggests that a portion of the microsphere must be exposed but they do not specifically teach a portion of the microsphere is exposed above the gelatin coating. However, Seul et al teach a similar method (¶ 18) wherein the microspheres are exposed above the gelatin coating thereby permitting a binding reaction between the binding agent on the microsphere and a target in solution (page 4, lines 3-6). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the microsphere exposure of Seul et al to the microspheres of Walt et al thereby exposing the microsphere for target binding as suggested by Walt et al (page 22, lines 20-22). One of ordinary skill in the art would have been motivated to expose the microspheres above the gelatin coating for the expected benefit of permitting target binding as taught by Seul et al (page 4, lines 3-6).

Regarding Claim 2, Walt et al disclose the method wherein each subpopulation has a unique optical signature (bar code) and a unique probe sequence (page 17, lines 15-19).

Regarding Claim 3, Walt et al disclose the method wherein the optical bar code is generated by two or more colorants i.e. each optical signature is comprises of a mixture of dyes (page 16, liens 25-28).

Regarding Claim 4, Walt et al disclose the method wherein the optical barcode is generated by a mixture of red, green and blue i.e. each optical signature is comprises of a mixture of dyes including red, green and blue dyes e.g. rhodamine, Malacite green, and Cascade Blue™ (page 16, line 25-page 17, line 2).

Regarding Claim 5, Walt et al disclose the method wherein at least one subpopulation has a luminescent property (i.e. fluorescence) and wherein detecting includes whole frame imaging capture of a resulting luminescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field

illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 6, Walt et al disclose the method wherein said processing uses a pattern recognition algorithm to obtain the identification (page 32, line 5-page 35, line 12).

Regarding Claim 7, Walt et al disclose the method wherein at least one subpopulation has a fluorescent property and wherein detecting includes whole frame imaging capture of a resulting fluorescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 8, Walt et al disclose the method wherein the substrate is characterized by an absence of specific sites capable of interaction physically or chemically with the microspheres i.e. a planar substrate or within a tube (page 7, liens 14-20).

Regarding Claim 9, Walt et al disclose the method wherein the microspheres bear surface active sites which contain the nucleic acid probe (page 14, lines 20-30).

Regarding Claim 10, Walt et al disclose the method wherein the microspheres have a mean diameter of between 1 and 50 microns (page 9, lines 21-23).

Regarding Claim 11, Walt et al disclose the method wherein the microspheres have a mean diameter of between 3 and 30 microns (page 9, lines 21-23).

Regarding Claim 12, Walt et al disclose the method wherein the microspheres have a mean diameter of between 5 and 20 microns (page 9, lines 21-23).

Regarding Claim 13, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 100 and 1 million microspheres per cm^2 (page 6, lines 21-24).

Regarding Claim 14, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 1,000 and 200,000 microspheres per cm^2 (page 6, lines 26-28).

Regarding Claim 15, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 10,000 and 100,00 microspheres per cm^2 (page 6, lines 21-28).

Regarding Claim 16, Walt et al disclose the method wherein the microspheres comprise a synthetic or natural polymeric material (page 9, lines 11-18).

Regarding Claim 17-18, Walt et al disclose the method wherein the microspheres comprise an amorphous polymer e.g. polystyrene (page 9, lines 11-18).

9. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (a) (WO 00/16101, published 23 March 2000) and Seul et al (U.S. Patent Application Publication No. 2003/0138842 A1 having priority to 60/300,025 filed 21 June 2001) as applied to Claim 1 and further in view of Walt et al (b) (U.S. Patent Application Publication No. 2002/0172716 A1, filed 25 October 2000).

Regarding Claim 19, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the

solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) but they do not teach the microsphere contains less than 30 percent crosslinking agent. However, Walt et al (b) teach microsphere composition whereby the amount of crosslinking agent determines microsphere pore size i.e. increasing amounts of crosslinking agents decreases pore size (¶ 7) and pores provide access to the hollow portion of the microsphere. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microspheres for entrapping dye of Walt et al (a) with a percent crosslinking agent which provides appropriate access to the hollow portion of the microsphere for dye entrapment as suggested by Walt et al (b) for the obvious benefit of entrapping the optical signature-specific dyes.

10. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) and Seul et al (U.S. Patent Application Publication No. 2003/0138842 A1 having priority to 60/300,025 filed 21 June 2001) as applied to Claim 1 and further in view of Chang et al (U.S. Patent No. 4,873,102, issued 10 October 1989).

Regarding Claim 20, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a

population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) but they are silent regarding the polymerization method. However, emulsion polymerization preparation of microspheres was well known in the art at the time the claimed invention was made as taught by Change et al (Example 1, Column 6, lines 25-57) wherein the method provides microspheres of very narrow size range. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the emulsion polymerization of Change et al to the microspheres of Walt et al to thereby provide microspheres of a uniform size as taught by Chang et al (Column 6, lines 26-28) for the obvious benefits of providing consistent microsphere surface area for surface interaction and thereby controlling interaction uniformity.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 21-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-25 of copending Application No. 10/036,828. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to method of identifying nucleic acid samples wherein the methods comprise very similar method steps which differ only in that the instantly claimed methods are limited to a fluorescently/chemiluminescently labeled target while the '828 claims are silent regarding a labeled target. However, the '828 specification specifically teach that the method includes fluorescently/chemiluminescently labeled targets (page 9, lines 8-26 and Fig. 7). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to fluorescently/chemiluminescently label the targets in the '828 method.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

NOTICE TO COMPLY WITH NUCLEIC ACID SEQUENCE RULES

13. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN a period of time which is co-extensive with the time to reply to the above Office Action WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
August 28, 2003